



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Thomas R. Cech et al.

Application No.: To Be Assigned

Filed: Herewith

For: HUMAN TELOMERASE  
CATALYTIC SUBUNIT: DIAGNOSTIC  
AND THERAPEUTIC METHODS

Examiner: To Be Assigned

Art Unit: To Be Assigned

INFORMATION DISCLOSURE  
STATEMENT UNDER 37 CFR §1.97 and  
§1.98

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. In accordance with 37 CFR §1.98(d), copies of the references can be found in Application No. 08/912,951, filed August 14, 1997 (Attorney Docket No. 015389-002600US). If the examiner would like additional copies of any of these cited references, applicants will happily provide them.

It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom. As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

Applicant believes that no fee is required for submission of this statement, since it is being submitted prior to the first Office Action. However, if a fee is required, the

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PATENT

Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



Hugh Wang  
Reg. No. 47,163

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PA 3194169 v1

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PTO/SB/08A (08-00)

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Substitute for form 1449A/PTO				<b>Complete if Known</b>	
				Application Number	To Be Assigned
				Filing Date	Herewith
				First Named Inventor	Cech, Thomas J.
				Group Art Unit	To Be Assigned
				Examiner Name	To Be Assigned
Sheet	1	of	10	Attorney Docket Number	015389-002640US



<b>U.S. PATENT DOCUMENTS</b>						
Examiner Initials *	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
A	08/751,189			Harrington, et al.	11/15/96	
B	60/038,750			Counter, et al.	02/20/97	
C	3,817,837			Tanenholz et al.	06-18-74	
D	3,850,752			Schuurs et al.	11-26-74	
E	3,939,350			Kronick et al.	02-17-76	
F	3,996,345			Ullman et al.	12-01-76	
G	4,275,149			Litman et al.	06-23-81	
H	4,277,437			Maggio	07-07-81	
I	4,366,241			Tom et al.	12-28-82	
J	4,683,195			Mullis et al.	07-28-87	
K	4,683,202			Mullis	07-28-87	
L	4,816,567			Cabilly et al.	03-28-89	
M	4,965,188			Mullis et al.	10-23-90	
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O	5,583,016			Villeponteau et al.	12-10-96	
P	5,747,317			Cao	05-05-98	
Q	5,770,422			Collins	06-23-98	
R	6,093,809			Cech, et al.	07/25/00	
S	6,258,535	B1		Villeponteau et al.	07/10/01	
T	6,261,556	B1		Weinrich et al.	07/17/01	
U	6,261,836	B1		Cech et al.	07/17/01	

<b>FOREIGN PATENT DOCUMENTS</b>								
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
V	JP	09154575-A				06-17-97		
W	PCT	WO 84/03564				09-13-84		
X	PCT	WO 95/13382				05-18-95		
Y	PCT	WO 96/01835				01-25-96		
Z	PCT	WO 96/12811				05-02-96		
AA	PCT	WO 96/19580				06-27-96		

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<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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AB	PCT	WO 96/40868				12-19-96		
AC	PCT	WO 98/01542				01-15-98		
AD	PCT	WO 98/01543				01-15-98		
AE	PCT	WO 98/07838				03-05-98		
AF	PCT	WO 98/08938				02-26-98		
AG	PCT	WO 98/21343				05-22-98		
AH	PCT	WO 98/37181				08-27-98		
AI	PCT	WO 98/45450				10-15-98		
AJ	PCT	WO 98/59040				12/30/98		
AK	PCT	WO 99/01560				01/14/99		

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Sheet	3	of	10	Attorney Docket Number	015389-002640US

<b>OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS</b>				
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.		T <sup>2</sup>
	AL	1994 Genome Issue of <i>Science</i> (265:1981f)		
	AM	Anderson and Young, "Quantitative Filter Hybridization" in <i>Nucleic Acid Hybridization</i> pp73-111 (1985)		
	AN	Ausubel <i>et al.</i> , <i>Current Protocols in Molecular Biology</i> , John Wiley & Sons, New York NY (1989)		
	AO	Autexier <i>et al.</i> , "Reconstitution of human telomerase activity and identification of a minimal functional region of the human telomerase RNA," (1996) <i>EMBO J</i> , 15:5928		
	AP	Auxerier and Greider, "Functional reconstitution of wild-type and mutant <i>Tetrahymena</i> telomerase," (1994) <i>Genes Develop.</i> , 8:563		
	AQ	Berger and Kimmel, <i>Guide to Molecular Cloning Techniques</i> , Meth. Enzymol., vol. 152, Academic Press, San Diego CA (1987)		
	AR	Blessman <i>et al.</i> , "Addition of Telomere-Associated HeT DNA Sequences "Heals" Broken Chromosome Ends in <i>Drosophila</i> ," (1990) <i>Cell</i> , 61:663		
	AS	Bitter <i>et al.</i> , "Expression and secretion vectors for yeast," Meth Enzymol., (1987) 153:516		
	AT	Blackburn and Chiou, "Non-nucleosomal packaging of a tandemly repeated DNA sequence at termini of extrachromosomal DNA coding for rRNA in <i>Tetrahymena</i> ," (1981) <i>Proc. Natl. Acad. Sci.</i> , 78:2263		
	AU	Blackburn and Gall, "A tandemly repeated sequence at the termini of the extrachromosomal ribosomal RNA genes in <i>Tetrahymena</i> ," (1978) <i>J. Mol. Biol.</i> , 120:33		
	AV	Blackburn, "Telomerases," (1992) <i>Ann. Rev. Biochem.</i> , 61:113		
	AW	Bodnar <i>et al.</i> , "Extension of Life-Span by Introduction of Telomerase into Normal Human Cells," (1998) <i>Science</i> , 279:349		
	AX	Bradford, "A Rapid and Sensitive method for the Quantitation of Microgram Quantities of Protein Utilizing the Principle of Protein-Dye Binding," (1976) <i>Anal. Biochem.</i> , 72:248		
	AY	Braunstein <i>et al.</i> , "Transcriptional silencing in yeast is associated with reduced nucleosome acetylation," (1993) <i>Genes Develop.</i> , 7:592		

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				First Named Inventor	Cech, Thomas J.
				Group Art Unit	To Be Assigned
				Examiner Name	To Be Assigned
Sheet	4	of	10	Attorney Docket Number	015389-002640US

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Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.		T <sup>2</sup>
	AZ	Calvio <i>et al.</i> , "Identification of hnRNP P2 as TLS/FUS using electrospray mass spectrometry," (1995) <i>RNA</i> , 1:724		
	BA	Caruthers <i>et al.</i> , "New chemical methods for synthesizing polynucleotides," (1980) <i>Nucleic Acids Res. Symp. Ser.</i> , 215:223		
	BB	Chan and Tye, "Organization of DNA sequences and replication origins at yeast telomeres," (1983) <i>Cell</i> , 33:563		
	BC	Colbere-Garapin <i>et al.</i> , "A new dominant hybrid selective marker for higher eukaryotic cells," (1981) <i>J. Mol. Biol.</i> , 150:1		
	BD	Cole <i>et al.</i> , "The EBV-hybridoma technique and its application to human lung cancer," Monoclonal Antibodies and Cancer Therapy, Alan R. Liss Inc., New York NY 77-96 (1985)		
	BE	Collins <i>et al.</i> , "Purification of Tetrahymena telomerase and cloning of genes encoding the two protein components of the enzyme," (1995) <i>Cell</i> , 81:677		
	BF	Conrad <i>et al.</i> , "RAP1 protein interacts with yeast telomeres in vivo: Overproduction alters telomere structure and decreases chromosome stability," (1990) <i>Cell</i> , 63:739		
	BG	Coombs, <i>Dictionary of Biotechnology</i> , Stockton Press, New York NY (1994)		
	BH	Cote <i>et al.</i> , "Generation of human monoclonal antibodies reactive with cellular antigens," (1983) <i>Proc. Natl. Acad. Sci.</i> , 80:2026		
	BI	Counter <i>et al.</i> , "The catalytic subunit of yeast telomerase," (1997) <i>Proc. Natl. Acad. Sci.</i> , 94:9202		
	BJ	Counter <i>et al.</i> , (1994) <i>Proc. Natl. Acad. Sci.</i> , 91:2900		
	BK	Creighton, <i>Proteins, Structures and Molecular Principles</i> , WH Freeman and Co, New York, NY (1983)		
	BL	Dieffenbach and Dveksler, <i>PCR Primer, a Laboratory Manual</i> , Cold Spring Harbor Press, Plainview NY (1995)		

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	BM	Duplaa <i>et al.</i> , "Quantitative analysis of polymerase chain reaction products using biotinylated dUTP incorporation," (1993) <i>Anal. Biochem.</i> , 212:229	
	BN	Fang <i>et al.</i> , "Oxytricha telomere-binding protein: separable DNA-binding and dimerization domains of the α-subunit," <i>Genes Develop.</i> 7:870 (1993) and Gray <i>et al.</i> , (1991) <i>Cell</i> 67:807	
	BO	Feng <i>et al.</i> , "The RNA Component of Human Telomerase," (1995) <i>Science</i> , 269:1236	
	BP	GenBank Accession No. AA281296	
	BQ	Genbank accession no. AA299878	
	BR	Genbank accession no. AA311750	
	BS	Gilley <i>et al.</i> , "Altering specific telomerase RNA template residues affects active site function," (1995) <i>Genes Develop.</i> , 9:2214	
	BT	Gottschling and Cech, "Chromatin Structure of the Molecular Ends of Oxytricha Mononuclear DNA: Phased Nucleosomes and a Telomeric Complex," (1984) <i>Cell</i> , 38:501	
	BU	Gottschling and Zakian, "Telomere proteins: specific recognition and protection of the natural termini of Oxytricha macronuclear DNA," (1986) <i>Cell</i> 47:195	
	BV	Grant <i>et al.</i> , <i>Meth Enzymol.</i> , (1987) 153:516-544	
	BW	Greenwood <i>et al.</i> , "Phylogenetic relationships within the class oligohymenophorea, phylum ciliphora, inferred from the complete small subunit rRNA gene sequences of <i>Colpidium campylum</i> , <i>Glaucoma chattoni</i> , and <i>Opisthонecta henneguyi</i> ," (1991) <i>J. Mol. Evol.</i> , 3:163	
	BX	Greider and Blackburn, "A telomeric sequence in the RNA of Tetrahymena telomerase required for telomere repeat synthesis," (1989) <i>Nature</i> , 337:331	
	BY	Greider and Blackburn, "Identification of a specific telomere terminal transferase activity in Tetrahymena extracts," (1985) <i>Cell</i> , 43:405	

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	BZ	Greider, "Telomerase is processive," (1991) <i>Mol. Cell. Biol.</i> , 11:4572		
	CA	Greider, "Telomere Length Regulation," (1996) <i>Ann. Rev. Biochem.</i> , 65:337		
	CB	Hampton et al., <i>Serological Methods a Laboratory Manual</i> , APS Press, St Paul MN (1990)		
	CC	Harrington et al., "A Mammalian Telomerase-Associated Protein," (1997) <i>Science</i> , 275:973		
	CD	Harrington et al., "Human telomerase contains evolutionarily conserved catalytic and structural subunits," (1997) <i>Genes Dev.</i> , 11:3109		
	CE	Hartman and Mulligan, "Two dominant-acting selectable markers for gene transfer studies in mammalian cells," (1988) <i>Proc. Natl. Acad. Sci.</i> , 85:8047		
	CF	Henderson and Blackburn, "An overhanging 3' terminus is a conserved feature of telomeres," (1989) <i>Mol Cell. Biol.</i> , 9:345		
	CG	Horn et al., "Synthesis of oligonucleotides on cellulose. Part II: design and synthetic strategy to the synthesis of 22 oligodeoxynucleotides coding for gastric inhibitory polypeptide (GIP)," (1980) <i>Nucleic Acids Res. Symp. Ser.</i> , 225-232		
	CH	Hudson et al., "An STS-based map of the human genome," (1995) <i>Science</i> , 270:1945		
	CI	Huse et al., "Generation of a large combinatorial library of the immunoglobulin repertoire in phage lambda," (1989) <i>Science</i> , 246:1275		
	CJ	Johnson et al., (1991) <i>Mol. Cell Biol.</i> 11:1		
	CK	Kilian et al., "Isolation of a candidate human telomerase catalytic subunit gene, which reveals complex splicing patterns in different cell types," (1997) <i>Hum. Mol. Genet.</i> , 6:2011		
	CL	Kipling and Cooke, "Hypervariable ultra-long telomeres in mice," (1990) <i>Nature</i> 347:400		
	CM	Klobutcher et al., "All gene-sized DNA molecules in four species of hypotrichs have the same terminal sequence and an unusual 3' terminus," (1981) <i>Proc. Natl. Acad. Sci.</i> , 78:3015		

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	CN	Koehler and Milstein, "Continuous cultures of fused cells secreting antibody of predefined specificity," (1975) <i>Nature</i> 256:495		
	CO	Kosbor et al., "The production of monoclonal antibodies from human lymphocytes," (1983) <i>Immunol. Today</i> 4:72		
	CP	Lamond and Sproat, (1994) "Isolation and Characterization of Ribonucleoprotein Complexes," pp103-140		
	CQ	Lamond et al., "Probing the structure and function of U2 snRNP with antisense oligonucleotides made of 2'-OMe RNA," (1989) <i>Cell</i> , 58:383		
	CR	Lendvay et al., "Senescence mutants of <i>Saccharomyces cerevisiae</i> with a defect in telomere replication identify three additional EST genes," (1996) <i>Genetics</i> , 144		
	CS	Lingler et al., "Purification of telomerase from Euplotes adeiculatus: requirement of a primer 3' overhang," (1996) <i>Proc. Natl. Acad. Sci.</i> , 93:10712		
	CT	Lingler et al., "Reverse transcriptase motifs in the catalytic subunit of telomerase," (1997) <i>Science</i> , 276:561		
	CU	Lingner et al., "Telomerase RNAs of different ciliates have a common secondary structure and a permuted template," (1994) <i>Genes Develop.</i> , 8:1984		
	CV	Lingner et al., "Telomerase and DNA End Replication: No Longer a Lagging Strand Problem?," (1995) <i>Science</i> 269:1533		
	CW	Lowy et al., "Isolation of transforming DNA: Cloning the hamster aprt gene," (1980) <i>Cell</i> , 22:817		
	CX	Lustig and Petes, Identification of yeast mutants with altered telomere structure," (1986) <i>Proc. Natl. Acad. Sci.</i> , 83:1398		
	CY	Maddox et al., "Elevated serum levels in human pregnancy of a molecule immunochemically similar to eosinophil granule major basic protein," (1983) <i>J. Exp. Med.</i> , 158:1211		
	CZ	Makarov et al., "Nucleosomal Organization of Telomere-Specific Chromatin in Rat," (1993) <i>Cell</i> , 73:775		
	DA	McEachern and Blackburn, "runaway telomere elongation caused by telomerase RNA gene mutation," (1995) <i>Nature</i> , 376:403		

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				First Named Inventor	Cech, Thomas J.
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				Examiner Name	To Be Assigned
				Attorney Docket Number	015389-002640US

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	DB	Melby <i>et al.</i> , "Quantitative measurement of human cytokine gene expression by polymerase chain reaction," (1993) <i>J. Immunol. Meth.</i> , 159:235		
	DC	Merrifield, "Solid phase peptide synthesis. I. The synthesis of a tetrapeptide," (1963) <i>J. Am. Chem. Soc.</i> , 85:2149		
	DD	Meyerson <i>et al.</i> , "hEST2, the Putative Human Telomerase Catalytic Subunit Gene, Is Up-Regulated in Tumor Cells and during Immortalization," (1997) <i>Cell</i> , 90:785		
	DE	Murray, <i>In McGraw Hill Yearbook of Science and Technology</i> , (1992) McGraw Hill, New York NY, pp 191-196		
	DF	Nakamura <i>et al.</i> , "Telomerase Catalytic Subunit Homologs from Fission Yeast and Human," (1997) <i>Science</i> , 277:955		
	DG	Nakayama <i>et al.</i> , "TLP1: A Gene Encoding a Protein Component of Mammalian Telomerase Is a Novel Member of WD Repeats Family," (1997) <i>Cell</i> , 88:875		
	DH	Nielsen <i>et al.</i> , (1993) "Peptide nucleic acids (PNAs): Potential antisense and anti-gene agents," <i>Anticancer Drug Des.</i> , 8:53		
	DI	Oka <i>et al.</i> , "Inverted terminal repeat sequence in the macronuclear DNA of <i>Styloynchia pustulata</i> ," (1980) <i>Gene</i> , 10:301		
	DJ	Olovnikov, "A theory of marginotomy: The incomplete copying of template margin in enzymic synthesis of polynucleotides and biological significance of the phenomenon," (1973) <i>J. Theor. Biol.</i> , 41:181		
,	DK	Orlandi <i>et al.</i> , "Cloning immunoglobulin variable domains for expression by the polymerase chain reaction," (1989) <i>Proc. Natl. Acad. Sci.</i> , 86:3833		
	DL	Prescott, "The DNA of ciliated protozoa," (1994) <i>Microbiol. Rev.</i> , 58:233		
	DM	Price, (1993) <i>Blood Rev.</i> , 7:127		
	DN	Rhodes <i>et al.</i> , "Transformation of maize by electroporation of embryos," (1995) <i>Meth. Mol. Biol.</i> , 55:12†		
	DO	Roberge <i>et al.</i> , "A strategy for a convergent synthesis of N-linked glycopeptides on a solid support," (1995) <i>Science</i> , 269:202		

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	DP	Romero and Blackburn, "A conserved secondary structure for telomerase RNA," (1991) <i>Cell</i> , 67:343		
	DQ	Sambrook <i>et al.</i> , Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview NY (1989)		
	DR	Sandell <i>et al.</i> , "Transcription of yeast telomere alleviates telomere position effect without affecting chromosome stability," (1994) <i>Proc. Natl. Acad. Sci.</i> , 91:12061		
	DS	Sanger <i>et al.</i> , "DNA sequencing with chain-terminating inhibitors," (1977) <i>Proc. Natl. Acad. Sci.</i> , 74:5463		
	DT	Scharf <i>et al.</i> , "Heat stress promoters and transcription factors," (1994) <i>Result Probl. Cell Differ.</i> 20:125		
	DU	Shampay and Blackburn, "Generation of telomere-length heterogeneity in <i>Saccharomyces cerevisiae</i> ," (1988) <i>Proc. Natl. Acad. Sci.</i> , 85:534		
	DV	Sheen and Levis, "Transposition of the LINE-like retrotransposon TART to <i>Drosophila</i> chromosome termini," (1994) <i>Proc. Natl. Acad. Sci.</i> , 91:12510		
	DW	Singer and Gottschling, "TLC1: Template RNA Component of <i>Saccharomyces cerevisiae</i> Telomerase," (1994) <i>Science</i> 266:404		
	DX	Starling <i>et al.</i> , "Extensive telomere repeat arrays in mouse are hypervariable," (1990) <i>Nucleic Acids Res.</i> , 18:6881		
	DY	Swanton <i>et al.</i> , "Arrangement of Coding and Non-coding Sequences in the DNA Molecules Coding for rRNAs in <i>Oxytricha</i> sp.," (1980) <i>Chromosoma</i> 77:203		
	DZ	Tommerup <i>et al.</i> , "Unusual chromatin in human telomeres," (1994) <i>Mol. Cell. Biol.</i> , 14:5777		
	EA	Trask, "Fluorescence <i>in situ</i> hybridization: application in cytogenetics and gene mapping," (1991) <i>Trends Genet.</i> , 7:149		
	EB	Verma <i>et al.</i> , "Human Chromosomes: A Manual of Basic Techniques," Pergamon Press, New York NY (1988)		
	EC	Watson, "Origin of concatemeric T7 DNA," (1972) <i>Nature New Biol.</i> , 239:197		

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	ED	Weinrich <i>et al.</i> , "Reconstitution of human telomerase with the template RNA component hTR and the catalytic protein subunit hTRT," (1997) <i>Nat. Genet.</i> , 17(4):498		
	EE	Wellinger <i>et al.</i> , "Origin activation and formation of single-strand TG <sub>1,3</sub> tails occur sequentially in late S phase on a Yeast linear plasmid," (1993) <i>Mol. Cell. Biol.</i> , 13:4057		
	EF	Wellinger <i>et al.</i> , "Saccharomyces Telomeres Acquire Single-Strand TG <sub>1,3</sub> Tails Late in S Phase," (1993) <i>Cell</i> 72:51		
	EG	Whitehead Institute/MIT Center for Genome Research, Genetic Map of the Mouse, Database Release 10, April 28, 1995		
	EH	Wigler <i>et al.</i> , "Transfer of purified herpes virus thymidine kinase gene to cultured mouse cells," (1977) <i>Cell</i> , 11:223		
	EI	Wigler <i>et al.</i> , "Transformation of mammalian cells with an amplifiable dominant-acting gene," (1980) <i>Proc. Natl. Acad. Sci.</i> , 77:3567		
	EJ	Winter and Milstein, "Man-made antibodies," (1991) <i>Nature</i> , 349:293		
	EK	Wright <i>et al.</i> , "Saccharomyces telomeres assume a non-nucleosomal chromatin structure," (1992) <i>Genes Develop.</i> , 6:197		
	EL	Yu <i>et al.</i> , "In vivo alteration of telomere sequences and senescence caused by mutated Tetrahymena telomerase RNAs," (1990) <i>Nature</i> , 344:126		
	EM	Zahler and Prescott, "Telomere terminal transferase activity in the hypotrichous ciliate <i>Oxytricha nova</i> and a model for replication of the ends of linear DNA molecules," (1988) <i>Nucleic Acids Res.</i> , 16:6953		
	EN	Zakian, Telomeres: Beginning to Understand the End," (1995) <i>Science</i> 270:1601		
	EO	Zaug <i>et al.</i> , "Catalysis of RNA Cleavage by a Ribozyme Derived from the Group I Intron of Anabaena Pre-tRNA <sup>Leu</sup> ,"		

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